REMARKS

Favorable consideration of this application is respectfully requested in view of the following remarks.

Claims 1-49 are pending in the application. The specification has been objected to and Claims 1-49 have been rejected. It is further noted that amendments have been made to the Drawings. Two replacement sheets for Figures 7-8 (A,B) which include changes at the bottom of Figures 7-8 (A,B) are attached hereto. These sheets replace the original sheets including Figures 7-8 (A,B). In the replacement sheet for Figure 7 (A,B) at the bottom, the two downward arrows and the phrase "Interfering signals of no differential expression" which appeared in original Figure 7 (A,B) have been omitted. In addition, in the replacement sheets at the bottom of Figures 7-8 (A,B), arrows have been added along the horizontal axis of the MALDI spectra. This change in Figures 7-8 (A,B) is supported in the specification on page 30 (Example 13). Further, in original Figures 7-8 (A,B) the two-way arrow appearing at "11 Da, 14 Da, 16 Da, 19 Da, 25 Da, 30 Da and 28 Da was a typographical error and has been replaced by a triangle sign in the replacement sheets for Figures 7-8 (A,B). No new matter has been added.

The Examiner has objected to the disclosure alleging that certain terms are indefinite. Specifically, the Examiner states:

On page 7, the paragraph beginning "Figure 2.", the sentence beginning "A 2-Da mass shift between (A) and (B)..." is indefinite because it is unclear how a mass shift is indicative of differential protein expression when the specification has not yet defined "differentially expressed."

On page 7, the paragraph beginning "Figure 3.", the sentence beginning "A 4-Da mass shift between (A) and (B)..." is indefinite because it is unclear how a mass shift is indicative of differential protein expression when the specification has not yet defined "differentially expressed."

The apparent interchangeable usage of the terms "inverse" (see e.g., p. 15, second paragraph, "the inverse should be observed...") "reversal" (see e.g. p. 11, first paragraph, "an isotope peak intensity ratio reversal..."), "converse" (see e.g., p. 11, second paragraph, "two converse collaborative labeling experiments...") and "inverted" (see e.g., p. 19, When the labeling is inverted...") is indefinite. Applicants are required to provide definitions for each of these terms, or provide correlation to art recognized definitions.

Appropriate correction is required.

Applicants disagree with the Examiner's objections and respectfully submit that the terms mentioned by the Examiner as being indefinite are definite for the reasons stated below.

With respect to the Examiner's contention that the term "differentially expressed" is not defined in the specification, the Examiner's attention is directed to the specification on page 10 under the heading "Description of the Invention." Therein, the specification expressly states

"The term "differentially expressed" with respect to protein(s) refers to quantitative changes in expression level as well as qualitative changes such as covalent changes, e.g., post-translational modifications such as protein phosphorylation, protein glycosylation, protein acetylation and protein processing of the C-or N-terminal of a protein."

Further, Figures 2A, 2B, 3A and 3B of the specification clearly show that for differentially expressed proteins (e.g., where BSA is "down-regulated" by 3-fold and aldolase is "upregulated" by 3-fold; see Example 6), there is a 2/4 mass shift of the more intense isotopic ion between the two inverse labeling experiments (Figures 2A,B, and Figures 3A,B). The observation of a 2/4 mass shift of the more intense isotopic ion between two inverse labeling experiments for differentially expressed proteins is also depicted in Figure 1 and discussed on page 19 of the specification. Since a definition of "differentially expressed" with respect to protein(s) is provided in the specification and the specification clearly shows and explains that a mass shift between the two inverse labeling experiments of the more intense isotopic ion is observed with differentially expressed proteins, the sentences objected to on page 7 are definite.

With respect to the term "inverse" at page 15, second paragraph ("...the inverse should be observed..."), the Examiner's attention is first directed to the definition of the term "inverse labeling pattern" on page 11 of the specification which means "a qualitative mass shift or an isotope peak intensity ratio reversal, i.e., from the heavy-labeled signal being stronger to the light-labeled signal being stronger (or vice versa) detected between the two inverse labeled mixtures." The Examiner's attention is also directed to the dictionary meaning of the term "inverse" which mean "opposite, reverse" (see Merriam-Webster's Collegiate Dictionary, 10th Ed., c. 1999, page 616, a copy of which is attached). Keeping these definitions in mind, the Examiner's attention is further directed to the complete sentence containing the term "inverse" at page 15, second paragraph, of the specification, which states,

"If expression of a protein has been up or down regulated, i.e, a true shift in signal intensities of the light isotope and heavy isotope is observed in the first mixture, the inverse should be observed in analyzing the second mixture due to inverse labeling."

In taking into consideration the definition of "inverse labeling pattern", the dictionary meaning of "inverse", and viewing the term "inverse" in context of the complete sentence on page 15 in which it appears, one skilled in the art would understand that the term "inverse"

means that there is a reversal in the signal intensities of the light and heavy isotope in the second mixture when compared with the signal intensities of the light and heavy isotopes in the first mixture. The meaning of "inverse" in the sentence on page 15 of the specification is further supported e.g., by Figure 1 depicting the inverse labeling experiment and discussion of this experiment on page 19 of the specification. Accordingly, one skilled in the art when ascertaining the meaning of the term "inverse" in the context of the complete sentence on page 15, second paragraph, in which this term appears, and the other description provided in the specification would consider the term "inverse" to be definite.

With respect to the term "reversal" (see e.g., page 11, first paragraph, "an isotope peak intensity ratio reversal..."), the Examiner's attention is directed to the complete sentence containing the phrase "isotope peak intensity ratio reversal." The complete sentence at page 11, first paragraph, explains the definition of the phrase "inverse labeling pattern" and further indicates that an isotope peak intensity ratio reversal means "from the heavy-labeled signal being stronger to the light-labeled signal being strong (or vice versa) detected between the two inverse labeled mixtures." The meaning of the term "isotope peak intensity ratio reversal" is further explained, e.g., on page 19 and shown in Figure 1 of the specification. Accordingly, one skilled in the art reading the complete sentence containing the phrase "isotope peak intensity ratio reversal" on page 11, first paragraph, together with the other disclosure provided in the specification would understand the meaning of the term "reversal" and would consider this term to be definite.

With respect to the term "converse" in the phrase "two converse collaborative labeling experiments" on page 11, second paragraph, the term "converse" has the same meaning as the term "inverse" contained in the phrase "inverse labeling experiments". In the context of the complete phrases which contain these words, ""converse labeling experiments" and "inverse labeling experiment", these phrases are explained, e.g., in the paragraph bridging pages 11-12 of the specification, which states

"... one protein pool from each of the reference and experimental samples is labeled with an isotopically heavy protein labeling reagent to provide an isotopically heavy-labeled reference pool and an isotopically heavy-labeled experimental pool. The remaining pool from each of the reference and experimental samples is labeled with an isotopically light protein labeling reagent to provide an isotopically light-labeled reference pool and an isotopically light-labeled experimental pool."

The specification e.g., on page 14, fourth paragraph, further states

Once labeling of the pools is completed, the isotopically light-labeled reference pool is combined with the isotopically heavy-labeled experimental pool to provide a first mixture. The

isotopically heavy-labeled reference pool is then combined with the isotopically light-labeled experimental pool to provide a second mixture. Accordingly, in the first mixture, the isotopically heavy-labeled proteins are derived from the experimental pool, whereas in the second mixture the isotopically heavy-labeled proteins are derived from the reference pool."

Accordingly, the specification on pages 11, 12 and 14 indicates that in the first and second mixtures which are used in the first and second experiments, respectively, the heavy and light labels are reversed in the reference and experimental pools. The synonymous meaning of the terms "converse" in the phrase "converse labeling experiment" and "inverse" in the phrase "inverse labeling experiment" is further supported e.g., by the explanation of this type of experiment in the specification, e.g., on page 19 and Figure 1 and in the definition of the term "converse" provided in Merriam-Webster's Collegiate Dictionary as "reversed in order" (see Merriam-Webster's Collegiate Dictionary on page 253, a copy of which is attached).

Accordingly, the term "converse" when considered in the context of the complete sentence in which it appears together with other disclosure provided in the specification and the dictionary meaning of the term "converse" is definite.

With respect to the term "inverted" (see e.g., p. 19, "When the labeling is inverted"), the Examiner's attention is directed to page 19, lines 16-21 of the specification which states:

..."For example, if a protein is substantially up-regulated by a disease state in pool 2 in comparison to the control pool 1, and when the disease sample is ¹⁸O, higher intensities of the ¹⁸O-signals for all peptides from this protein will be observed except for the C-terminal peptide. When the labeling is **inverted** in the second experiment in which the control pool is ¹⁸O-labeled while the disease pool is not labeled, the ¹⁶O-signal will be stronger for those peptides.

Accordingly, the specification indicates that when in the first experiment, a disease pool is labeled with a heavy isotope and combined with a control pool labeled with a light isotope, i.e., ¹⁶O, then in the second experiment, the label is inverted (reversed), i.e., the control pool is labeled with the heavy isotope and combined with the disease pool labeled with the light isotope. In other words, the labeling of the reference and experimental pools in the first experiment is reversed or inverted in the second experiment. This meaning of inverted is also supported by the description pertaining to labeling of the pools found on pages 11, 12 and 14 of the specification as discussed above.

It is further noted that the term "inverted" is defined in the Merriam-Webster's Collegiate Dictionary on page 616 (a copy of which is attached) as "reversed."

Accordingly, one skilled in the art reading the term "inverted" in the context of the sentences and paragraph in which it appears together with other disclosure provided in the specification and the dictionary meaning of the term "inverted" would consider this term to be definite.

In sum, the aforementioned terms "inverse", reversal, converse and inverted" are definite when viewed in the context of the sentence in which they appear, the description provided in the specification and the dictionary meaning of these terms.

In view of the above, withdrawal of the objections raised by the Examiner is respectfully requested.

Claims 1-49 have been provisionally rejected under 35 U.S.C. §101 as claiming the same invention as that of Claims 1-49 of co-pending Application No. 10/412,964. In response, Claims 1-49 of co-pending Application No. 10/412,964 have been cancelled without prejudice (see attached amendment submitted for co-pending Application No. 10/412,964.).

In view of the above, withdrawal of the provisional rejection of Claims 1-49 under 35 U.S.C. §101 is respectfully requested.

A good faith effort has been made to place the present application in condition for allowance. If the Examiner believes a telephone conference would be of value, he is requested to call the undersigned at the number listed below.

Respectfully submitted,

Attorney for Applicants

Susan Hess

Reg. No. 37,350

Novartis Corporate Intellectual Property One Health Plaza, Building 104 East Hanover, NJ 07936-1080 (862) 778-7859

Date: December 8, 2004

Attachments

Amendments to the Drawings:

The two attached sheets of drawings include changes to Figures 7-8 (A,B). These sheets which include Figures 7-8 (A,B) replace the original sheets including Figures 7-8 (A,B). In the replacement sheet for Figure 7 (A,B) at the bottom, the two downward arrows and the phrase "Interfering signals of no differential expression" which appeared in original Figure 7 (A,B) have been omitted. In addition, in the replacement sheets for Figures 7-8 (A,B) at the bottom, arrows have been added along the horizontal axis of the MALDI spectra. Further, in original Figures 7-8 (A,B) the two-way arrow appearing at "11Da, 14Da, 16 Da, 19 Da, 25 Da, 30 Da and 28 Da" was a typographical error and has been replaced by a triangle sign in the replacement sheets for these two figures.

Attachment: Two Replacement Sheets



IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF YANGOI KAREN WANG

APPLICATION NO: 10/412,964

FILED: APRIL 14, 2003

FOR: INVERSE LABELING METHOD FOR THE RAPID IDENTIFICATION

OF MARKER/TARGET PROTEINS

MS: Amendment Commissioner for Patents PO Box 1450 Alexandria, VA 22313-1450

AMENDMENT

Sir:

Prior to the examination of this application, please amend the application as follows:

Amendments to the claims begin on page 2 of this paper

Remarks begin on page 8 of this paper.

Amendments to the claims:

Claims 1 - 49 (cancelled)

Claim 50. (original) A method for preparing and purifying peptides from a solution comprising proteins, the method comprising:

- a) subjecting the solution comprising proteins to molecular filtration using a first filtration membrane to obtain a retentate comprising proteins;
- b) chemically or enzymatically cleaving the proteins in the retentate to obtain peptides; and
- c) subjecting the peptides in the retentate to molecular filtration utilizing a second filtration membrane to obtain a filtrate comprising peptides, wherein the second filtration membrane has a molecular weight cutoff smaller than or equal to the molecular weight cutoff of the first filtration membrane utilized in Step (a).

Claim 51. (original) The method of Claim 50, wherein the solution comprising proteins is obtained from a sample selected from the group consisting of a protein overexpressed in cells that is in the form of inclusion bodies or secreted from the cell, cell homogenates, cell fractions, tissue homogenates, immunoprecipitates, biological fluids, tears, feces, saliva and lavage fluids.

Claim 52. (original) The method of Claim 50, wherein the first and second filtration membranes have a molecular weight cutoff of from about 3 kD to about 50 kD.

Claim 53. (original) The method of Claim 52, wherein the first and second filtration membranes have a molecular weight cutoff of about 10 kD.

Claim 54. (original) The method of Claim 50, wherein the step of enzymatically cleaving the proteins is performed using a protease selected from the group consisting of trypsin, chymotrypsin, endoproteinase Lys-C, endoproteinase Glu-C, endoproteinase Asp-N, endoproteinase Arg-C and combinations thereof.

Claim 55. (original) The method of Claim 50, wherein the proteins are phosphorylated proteins and the peptides are phosphorylated peptides.

Claim 56. (original) The method of Claim 50, which further comprises labeling the peptides in the filtrate.

Claim 57. (original) The method of Claim 50, which further comprises subjecting the solution comprising proteins to at least one fractionation technique to reduce the complexity of proteins in the solution.

Claim 58. (original) The method of Claim 57, wherein the fractionation technique is selected from the group consisting of ammonium sulfate precipitation, isoelectric focusing, size exclusion chromatography, ion exchange chromatography, adsorption chromatography, reverse phase liquid chromatography, affinity chromatography, immunoprecipitation and combinations thereof.

Claim 59. (original) The method of Claim 50, which further comprises subjecting the filtrate comprising peptides to at least one fractionation technique to reduce the complexity of the peptides in the filtrate.

Claim 60. (original) The method of Claim 59, wherein the fractionation technique is selected from the group consisting of size exclusion chromatography, ion exchange chromatography, adsorption chromatography, reverse phase liquid chromatography, affinity chromatography immunoprecipitation and combinations thereof.

Claim 61. (original) The method of Claim 60, wherein the fractionation technique is affinity chromatography.

Claim 62. (original) A method for preparing and purifying phosphorylated peptides from a solution comprising phosphorylated and non-phosphorylated proteins, the method comprising:

- a) subjecting the solution to molecular filtration utilizing a first filtration membrane to obtain a retentate comprising phosphorylated and non-phosphorylated proteins;
- b) chemically or enzymatically cleaving the proteins in the retentate to produce phosphorylated and non-phosphorylated peptides;
- c) subjecting the peptides in the retentate to molecular filtration utilizing a second filtration membrane to obtain a filtrate comprising phosphorylated and non-phosphorylated peptides, wherein the second filtration membrane has a molecular weight cutoff smaller than or equal to the molecular weight cutoff of the first filtration membrane;
- d) loading the filtrate onto an affinity column, wherein the phosphorylated peptides in the filtrate bind to the affinity column and the non-phosphorylated peptides in the filtrate flow through the affinity column; and
- e) eluting the bound phosphorylated peptides from the affinity column.

Claim 63. (original) The method of Claim 62, wherein the first and second filtration membranes have a molecular weight cutoff of from about 3 kD to about 50 kD.

Claim 64. (original) The method of Claim 63, wherein the first and second filtration membranes have a molecular weight cutoff of about 10 kD.

Claim 65. (original) The method of Claim 62, wherein the affinity column is an immobilized metal affinity column.

Claim 66. (original) The method of Claim 62, wherein the step of eluting the bound phosphorylated peptides from the immobilized metal affinity column is carried out using an organic solvent/water mixture.

Claim 67. (original) The method of Claim 66, wherein the pH of the organic solvent/water mixture is from about 9 to about 10.

Claim 68. (original) The method of Claim 62, wherein the phosphorylated and non-phosphorylated peptides in the filtrate are esterified prior to the step of loading the filtrate onto the immobilized metal affinity column.

Claim 69. (original) The method of Claim 62, which further comprises labeling the peptides in the filtrate prior or subsequent to the step of loading the filtrate onto the affinity column.

Claim 70. (original) A method for identifying a differentially-expressed protein in two different samples containing a population of proteins, the method comprising:

- a) subjecting a reference sample and an experimental sample to molecular filtration using a first filtration membrane to obtain a reference sample comprising proteins and an experimental retentate comprising proteins;
- b) chemically or enzymatically cleaving the proteins in each of the reference and experimental retentates to obtain peptides;
- c) subjecting the peptides in the reference and experimental retentates to molecular filtration using a second filtration membrane to obtain a reference filtrate comprising peptides and an experimental filtrate comprising peptides, wherein the second filtration membrane has a molecular weight cutoff smaller than or equal to the molecular weight cutoff of the first filtration membrane;
- d) providing two equal peptide pools from each of the reference and experimental filtrates;
- e) labeling the peptide pools with a substantially chemically identical isotopically different labeling reagent; wherein one pool from each of the reference and experimental pools is labeled with an isotopically heavy labeling reagent to provide an isotopically heavy-labeled reference pool and an isotopically heavy-labeled experimental pool, and wherein the remaining reference and experimental pools are labeled with an isotopically light labeling reagent to provide an isotopically light-labeled reference pool and an isotopically light-labeled experimental pool;

- f) combining the isotopically light-labeled reference pool with the isotopically heavylabeled experimental pool to provide a first peptide mixture;
- g) combining the isotopically heavy-labeled reference pool with the isotopically lightlabeled experimental pool to provide a second peptide mixture;
- h) detecting the labeled peptides from each of the two peptide mixtures; and
- i) comparing the labeling pattern obtained from the labeled peptides in the first and second mixtures, wherein an inverse labeling pattern of a peptide in the second mixture compared with the labeling pattern of the peptide in the first mixture is indicative of the differentially-expressed protein in the two different samples.

Claim 71. (original) The method of Claim 70, wherein the samples are selected from the group consisting of cell homogenates, cell fractions, tissue homogenates, biological fluids, tears, feces, saliva and lavage fluids.

Claim 72. (original) The method of Claim 71, wherein the two samples differ in cell type, tissue type, physiological state, disease state, developmental stage, environmental conditions, nutritional conditions, chemical stimuli or physical stimuli.

Claim 73. (original) The method of Claim 70, which further comprises subjecting the samples to at least one fractionation technique to reduce the complexity of proteins in the samples prior to Step (a).

Claim 74. (original) The method of Claim 70, wherein the steps of molecular filtration utilize a filtration membrane having a molecular weight cutoff of from about 3 kD to about 50 kD.

Claim 75. (original) The method of Claim 74, wherein the steps of molecular filtration utilize a filtration membrane having a molecular weight cutoff of about 10 kD.

Claim 76. (original) The method of Claim 70, wherein the isotopically heavy protein labeling reagent contains a stable heavy isotope selected from the group consisting of ²H, ¹³C, ¹⁵N, ¹⁷O, ¹⁸O and ³⁴S.

Claim 77. (original) The method of Claim 70, wherein the isotopically light protein labeling reagent contains a stable light isotope selected from the group consisting of H, ¹²C, ¹⁴N, ¹⁶O and ³²S.

Claim 78. (original) The method of Claim 70, wherein the isotopically heavy protein labeling agent labeling reagent is d3-methanolic HCl and the isotopically light protein labeling reagent is d0-methanolic HCl.

Claim 79. (original) The method of Claim 70, further comprising separating the peptides in the two peptide mixtures prior to Step (h).

Claim 80. (original) The method of Claim 79, wherein the step of separating the labeled peptides in the two peptide mixtures is carried out using a technique selected from the group consisting of size exclusion chromatography, ion exchange chromatography, adsorption chromatography, reverse phase chromatography, affinity chromatography, immunoprecipitation and combinations thereof.

Claim 81. (original) The method of Claim 70, wherein the differentially-expressed protein is a phosphorylated protein and the labeled peptides in each of the two mixtures are phosphorylated peptides and non-phosphorylated peptides.

Claim 82. (original) The method of Claim 70, further comprising the step of separating the phosphorylated peptides from the non-phosphorylated peptides.

Claim 83. (original) The method of Claim 82, wherein the step of separating labeled phosphorylated peptides from labeled non-phosphorylated peptides comprises:

- i) loading the labeled peptides onto an affinity column, wherein the labeled phosphorylated peptides bind to the affinity column and the non-phosphorylated peptides flow through the affinity column; and
- ii) eluting the phosphorylated peptides from the affinity column.

Claim 84. (original) The method of Claim 83, wherein the affinity column is an immobilized metal affinity column.

Claim 85. (original) The method of Claim 84, which further comprises esterifying the labeled peptides from the first and second mixtures prior to loading the peptides onto the immobilized affinity column.

Claim 86. (original) The method of Claim 84, wherein labeling of the peptides is carried out utilizing a labeled esterification reagent prior to loading the labeled peptides onto the immobilized affinity column.

Claim 87. (original) The method of Claim 70, wherein the labeled peptides are detected by MS.

Claim 88. (original) The method of Claim 70, which further comprises sequencing one of the peptides to identify the differentially-expressed protein from which the peptide originated.

Claim 89. (original) The method of Claim 88, wherein sequencing of the peptide is performed utilizing MS/MS or PSD.

Remarks

In response to the provisional rejection of Claims 1-49 in parent Application Serial No. 10/016,627 under 35 U.S.C. §101 as claiming the same invention as that of Claims 1-49 in the present application, Claims 1-49 of the present application have been cancelled without prejudice. Early examination of the claims and allowance of the same are respectfully requested.

Respectfully submitted,

Attorney for Applicant

Reg. No. 37,350

Novartis Corporate Intellectual Property One Health Plaza, Building 104 East Hanover, NJ 07936-1080 (862) 778-7859

Date: December 3, 2004



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Collegiate Dictionary

TENTH EDITION

Merriam-Webster, Incorporated Springfield, Massachusetts, U.S.A.

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9 inverse n (ca. 1681) 1: something of a contrary n (ca. 1681) 1: something or quality
9 inverse n (ca. 1681) 1: something or quality in such a way that the result of applying a given binary operation to them is an identity element of the set inverse function n (1816): a function that is derived from a given function by interchanging the two variables — compare LOGARITHMIC inverse-ly \'in-,vors-le, ()in \' adv (1660) 1: in an inverse order or manner 2: in the manner of inverse variation (varies -> inversely proportional adj (ca. 1890): related by inverse variation compare DIRECTLY PROPORTIONAL inverse square law n (1921): a statement in physics: a given physical quantity (as illumination) varies with the distance from the source inversely as the square of the distance quantity (as illumination) varies with the distance from the source inversely as the square of the distance inverse variation n (1936) 1: mathematical relationship between two variables which can be expressed by an equation in which the product of two variables is equal to a constant 2: an equation or function expressing inverse variation—compare DIRECT VARIATION in-ver-sion \in-ver-zhən, -shən\ n (1586) 1: a reversal of position, order, form, or relationship as a (1): a change in normal word order; esp: the placement of a verb before its subject (2)! the process or result of changing or reversing the relative positions of the notes of a musical interval, chord, or phrase b: the condition of being turned insaid interval, chord, or phrase b: the condition of being turned insusal or inside out c: a breaking off of a chromosome section and its subsequent reattachment in inverted position; also: a chromosomal section that has undergone this process. 2: the act or process of inverting a: a change in the order of the terms of a mathematical proportion effected by inverting each ratio b: the operation of forming the inverse of a magnitude; a function, an operation, or an element 4 a: the conversion of dextrorotatory sucrose into a levorotatory mixture of glucose and fructose -b: a change from one stereochemical figuration at a chiral center in a usu. organic molecule to the opposite configuration that is brought about by a reaction in which a substitution of one group is made for a different group 5: thomosexuality 6: (an increase of temperature with height through a layer of air in-ver-sive \(\text{-vor-siv}, -ziv\) adj (1875): marked by inversion

worth vort v. [Linvertere from wentere to unn to worth] (1533) 1 at to reverse in position; order or relation to subject to inversion, 2 at to turn inside out or upside to turn inward, 3 to find the mathematical reciprocal of (using fractions, the divisor and multiply) synisee Reversions in vert vin vert vin (1838); one characterized by inversion (Mosexual) in-vert \(\) in-vort\\\ n_1(1838)_{\text{iii}}\) one characterized by inversion if MOSEXUAL in-vortase \(\) in vortase \(\) in-vortase \(\) in Invert sugar n (1880): a mixture of dextrose and levillose of fruits or produced artificially by the inversion of sucrose linvest \in vest\ v (L investire to clothe, surround fr. Ingarment — more at wear can 1534): 1 [ML investire fr. L. 1534]: 1 invest vb [it investire to clothe, invest money, fr. L. to clothe] pi(1 it to commit (money) in order to earn a financial return 2 it (money) in order to earn a financial return 2 it (money) in order to earn a financial return 2 it (money) in order to earn a financial return 2 it (money) in order to earn a financial return 2 it (money) in vest able \(\frac{1}{2}\text{ves-to-bol-adj-in-ves-to-far-langle}\) in vest able \(\frac{1}{2}\text{ves-to-bal-adj-in-ves-to-far-langle}\) in vest (money) in vest (money adj — In-ves-ti-ga-tor V-ga-tor \n.— In-ves-ti-ga-tor \n/\display
itōr-e, -tor-\adj
in-ves-ti-ture \n-\ves-ta-chur, -chor, -tyur, -tur\n [ME tr-ML
ittura, fr. investitus, pp. of investire] (14c) 1; the act of establish
office or ratifying 2: something that covers or adorns
lin-vest-ment \n-\ves(t)-mont\n [\linvest] (1597) 1; a archaic westMENT b: an outer layer: ENVELOPE 2: INVESTITURE 1 3: BLOCK
SIEGE Siege 2 investment n [?invest] (1615): the outlay of money usu. for incomprofit: capital outlay; also: the sum invested of the property in profit: capital outlay; also: the sum invested of the propertyl chased investment company n (ca. 1917): a company whose primary beness is holding securities of other companies purely for investing purposes; compare HolDing company:

in-vete-ra-cy \in-ve-t(-)-ra-se\ n [inveterate + cy] (ca. 1719) (quality or state of being obstinate or persistent: TENACITY inveterate \in-ve-t(-)-ra-vet \(\frac{1}{2} \) (The first \(\frac{1}{2} \) (ME, [n L. inveterate \in-ve-t(-)-ra-vet \(\frac{1}{2} \) (ME, [n L. inveterate \in-ve-t(-)-ra-vet \(\frac{1}{2} \) (me) confirmed by long, persistence (the \(\sigma \) tendency to overlethe obvious. \(\frac{1}{2} \) confirmed in a habit: HABITUAL (an \sigma \) liar \(\frac{1}{2} \) inveterate ly adv

Syn inveterate \(\frac{1}{2} \) overlether ate \(\frac{1}{2} \) overlether ate \(\frac{1}{2} \) yet \(\frac{1}{2} \) of the obvious. \(\frac{1}{2} \) confirmed in a habit: HABITUAL (an \sigma \) liar \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) of the obvious \(\frac{1}{2} \) confirmed in a habit: HABITUAL (an \sigma \) liar \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) of the obvious \(\frac{1}{2} \) confirmed in a habit: HABITUAL (an \sigma \) liar \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) of the obvious \(\frac{1}{2} \) confirmed in a habit: HABITUAL (an \sigma \) liar \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) of the obvious \(\frac{1}{2} \) confirmed in a habit: HABITUAL (an \sigma \) liar \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) of the obvious \(\frac{1}{2} \) confirmed in a habit: HABITUAL (an \sigma \) liar \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) of the obvious \(\frac{1}{2} \) of the obvious \(\frac{1}{2} \) confirmed in a habit: HABITUAL (an \sigma \) liar \(\frac{1}{2} \) inveterate \(\frac{1}{2} \) invete that is persistent or endlessly recurrent and troublesome (a chro complainer). in vi a ble \() in vi a bil\(adj [ISV] (1918) : incapable of survivi esp because of a deleterious genetic constitution — In vi a bil (1) \(\frac{1}{2}\text{vi-3-bi-la-te\) n in-vid-i-ous \(\text{in-vi-de-os\}\) adj \([L\)\) in-vid-ious \(\text{in-vi-de-os\}\) adj \([L\)\)\ in-vid-ious \(\text{in-vi-de-os\}\) adj \([L\)\)\ in-vid-ious \(\text{envi-de-os\}\)\ adj \([L\)\)\ in-vid-ious \(\text{envi-de-os\}\)\ adj \([L\)\)\ in-vid-ious \(\text{envi-de-os\}\)\ atsilon \(\text{envi-de-os\ unpleasant or objectionable nature: OBNOXIOUS (~ remarks), b. d. kind to cause harm or resentment (an ~ comparison) — in vidious ly adv — in vidi-ious-ness n in vigi-ilate \in-vi-j-, lat\ vb -lat-ed; -lat-ing [L invigilates pp. () invigilare to stay awake, be watchful, fr. in + vigilare to stay, awake more at vioilant] vi (1553): to keep watch; esp. Brit; to stay, awake students at an examination — vi : Supervise Monitor — in-vigilation\,\vi-vi-j-, la-toi\ n = in-vigilation\,\vi-vi-j-j-, la-toi\,\vi-vi-j-j-, la-toi\,\vi-vi-j-j-, la-toi\,\vi-vi-j-j-, la-toi\ n = in-vigilation\,\vi-vi-j-j-, la-toi\,\vi-vi-j-j-, la-toi\,\vi-vi D (1). < sə-bi-lə-tē\ n — in-vin-ci-ble-ness \\-'vin(t)-sə-bəl-nəs\ n — in-vin-cb bly \-ble\ adv. in visolate visolate in visolate in visolate in visolate visolate in visolate in visolate vis

AVAILABL

ntroven. com- | vt (14c) form or utensils ': MAN

o<u>llen,</u> fi AL con 2) 1 u b: to a: to to have esp. to

trol·la-:rolling use of a ation of 1 in pl a (1)

ехрегіest and imental ganism. hanism itus, or perfor-

DLLER 2 titution ship\ n

ated by

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on-troıl -sies de. lit..

by the 19): to - con-

: stub-

m-tu-ma-cy \kən-'tü-mə-sē, -'tyü-; 'kän-tü-, -tyü-, -chə-\ n [ME con-macie, fr. L contumacia, fr. contumac-, contumax rebellious] (13c) toubborn resistance to authority; specif: willful contempt of court ne-tu-me-li-ous \kän-tü-mē-lē-əs, -tyü-', -chə-\ adj (15c): insolunty abusive and humiliating — con-tu-me-li-ous-ly adv — tu-me-ly \kän-tü-mə-lē, kən-, -'tyü-; 'kän-tü-mē-lē, -tyü-, -chə-; in flumlet' 'kän-()tyüm-lē or 'kän-chəm-\ n, pl -lies [ME contumelie, fr. Mt. fr. L contumelia] (14c): harsh language or treatment arising from language on treatment arising from flumlet in the supplementation of such language or treatment arising from flumlet in the supplementation of such language or treatment arising from flumlet in the supplementation of such language or treatmentation.

fon tu-sion \kən-'tü-zhən, -'tyü-\ n [ME conteschown, fr. MF contu-tion, fr. L contusion-, contusio, fr. contundere to pound, bruise, fr. com-tundere to beat; akin to Goth stautan to strike, Skt tudati he pushes] | | \ | : injury to tissue usu. without laceration: BRUISE la -

h-in...-tyüz/ vt

nun-drum \kə-'nən-drəm\ n [origin unknown] (1645) 1: a riddle

hose answer is or involves a pun 2 a: a question or problem hav
ing only a conjectural answer b: an intricate and difficult problem

ton-ur-ba-tion \kä-(nər-'bā-shən\ n [com- + L urb-, urbs city] (1915)

an aggregation or continuous network of urban communities

n-nus ar-te-ri-o-sus \'kō-nəs-är-,tir-ē-'ō-səs\ n, pl co-ni ar-te-ri-o-si
\n.ni-ir-,tir-ē-'ō-si\ [NL, lit., arterial cone] (ca. 1860) 1: a conical

prolongation of the right ventricle in mammals from which the pulmo
hav arteries emerge — called also conus 2: a prolongation of the

ventricle of amphibians and some fishes that has a spiral valve separat
have nous blood going to the respiratory arteries from blood going to ing venous blood going to the respiratory arteries from blood going to

the norta and systemic arteries

non-va-lesce \(\), kän-va-les\\ vi -lesced; -lesc-ing [L convalescere, fr. from + valescere to grow strong, fr. valere to be strong, be well — from + valescere to grow strong, fr. valere to be strong, be well — from + valescere to grow strong, fr. valere to be strong, be well — from + valescere to grow strong, fr. valere to be strong, be well — from the valence of the valenc

convenience \kən-\vēn-yen\ vb con-vened; con-ven-ing [ME, fr. MF convenience \kən-\vēn\ vb con-vened; con-ven-ing [ME, fr. MF convenience \kən-\vēn\ vb con-vener vc (15c): to come together in a body of the convenience \kən-\vēn-yen (15c): to come together in a body of the convenience \kən-\vēn-yen (15c): to come together in a body of the convenience \kən-\vēn-yen (15c): to come together in a body of the convenience \kən-\vēn-yen (15c): to come together in a body of the convenience \kən-\vēn-yen (15c): to come together in a body of the convenience \kenueling (15c): to

use (~ foods)

convenience store n (1965): a small often franchised market that is

convenience store n (1965): a small often franchised market that is open long hours
conveniency \-yon(t)-se\ n (1601) archaic: CONVENIENCE
conve-nient \kon-\vec{ven}-yont\ adj [ME, fr. L convenient, conveniens, fr.
typ. of convenire to come together, be suitable, fr. com- + venire to
come — more at COME] (14c) 1 obs: SUITABLE, PROPER 2 a: suited
to personal comfort or to easy performance b: suited to a particular
stuation c: affording accommodation or advantage 3: being near
at hand: HANDY — con-ve-nient-ly adv
tron-vent \kan-v=nt, -v=nt\ n [ME covent, fr. OF, fr. ML conventus, fr.
i assembly, fr. convenire] (13c): a local community or house of a
religious order or congregation; esp: an establishment of nuns
tron-vent \kan-\vent\ vb [L conventus, pp. of convenire] (1514) obs

run-ven-ti-cle \kən-'ven-ti-kəl\ n [ME, fr. L conventiculum, dim. of conventisele \kn-ven-ti-kal\ n [ME, fr. L convententum, alm. of conventus assembly] (14c) 1: ASSEMBLY, MEETING 2: an assembly of an irregular or unlawful character 3: an assembly for religious worship: esp: a secret meeting for worship not sanctioned by law 4 | MEETINGHOUSE — conventi-cler \-k(x-)lar\ n | convention \kan-ven(t)-shan\ n [ME, fr. MF or L; MF, fr. L convention-conventio, fr. convenire] (15c) 1 a: AGREEMENT, CONTRACT b | an agreement between states for regulation of matters affecting all of

tan agreement between states for regulation of matters affecting all of them c: a compact between opposing commanders esp. concerning prisoner exchange or armistice d: a general agreement about basic principles or procedures; also: a principle or procedure accepted as true or correct by convention 2 a: the summoning or convening of an assembly b: an assembly of persons met for a common purpose; exp: a meeting of the delegates of a political party for the purpose of formulating a platform and selecting candidates for office c: the usustate or national organization of a religious denomination 3 a: usage or custom esp. in social matters b: a rule of conduct or behavior c: a practice in bidding or playing that conveys information between partners in a card game (as bridge) d: an established technique, practice, or device (as in literature or the theater)

conventional \ksin-\venture venth-nol, -\vent(t)-sh-n^2\lambda dj (15c) 1: formed by agreement or compact 2 a: according with, sanctioned by, or based on convention b: lacking originality or individuality: TRITE c (1): ORDINARY, COMMONPLACE (2): NONNUCLEAR 1 (~ warfare) 3 a nacording with a mode of artistic representation that simplifies or provides symbols or substitutes for natural forms b: of traditional

con-ven-tion-al-i-ty \-,ven(t)-sho-'na-lo-tē\ n, pl-ties (ca. 1834) 1: a conventional usage, practice, or thing 2: the quality or state of being conventional; esp: adherence to conventions con-ven-tion-eer \kon-,ven(t)-sho-'nir\ n (1926): a person attending a

convention

'con-ven-tu-al \kən-'ven-chə-wəl, kän-, -'vench-wəl\ adj [ME, fr. MF or ML; MF, fr. ML conventualis, fr. conventus convent] (15c) 1: of, relating to, or befitting a convent or monastic life: MONASTIC 2 cap: of or relating to the Conventuals — con-ven-tu-al-ly adv

'conventual n (1533) 1 cap: a member of the Order of Friars Minor Conventual forming a branch of the first order of St. Francis of Assist

Conventual forming a branch of the first order of St. Francis of Assist under a mitigated rule 2: a member of a conventual community converge \kan-'vorj\ vb converged; converging [LL converger, fr. L com- + vergere to bend, incline — more at WRENCH] vi (1691) 1: to tend or move toward one point or one another: come together is MEET 2: to come together and unite in a common interest or focus 3: to approach a limit as the number of terms increases without limit

3: to approach a limit as the number of terms increases without limit

vi: to cause to converge

conver-gence \kon-vər-jən(t)s\ n (1713) 1: the act of converging
and esp. moving toward union or uniformity; esp: coordinated movement of the two eyes so that the image of a single point is formed on
corresponding retinal areas 2: the state or property of being convergent 3: independent development of similar characters (as of bodily
structure or cultural traits) often associated with similarity of habits or
environment.

environment conver-gen-cy \-jan(t)-s\\ n (1709): CONVERGENCE conver-gent \-jant\ adj (ca. 1751) 1: tending to move toward one point or to approach each other: CONVERGING $\langle \sim \text{lines} \rangle$ 2: exhibiting convergence in form, function, or development $\langle \sim \text{convincion} \rangle$ 3 as of an improper integral: having a value that is a real number b: characterized by having the nth term or the sum of the first n terms approach a finite limit (a $\sim \text{sequence} \rangle \langle a \sim \text{series} \rangle$

approach a limit mint (a \sim sequence) (a \sim series) converging lens n (1860): a lens that causes parallel rays (as of light)

to come to a focus con-vers-able \kan-\var-sa-bal\ adj (ca. 1631) 1 archaic: relating to or suitable for social interaction 2: pleasant and easy to converse

con-ver-sance \kən-'vər-san(t)s also 'kän-vər-san(t)s\ n (1609): the

quality or state of being conversant

con-ver-san-cy \-s^n(t)-sē, -sən(t)-\ n (1798): CONVERSANCE

con-ver-sant \kən-\vər-s\nt also \kän-vər-sənt\ adj (14c) 1 archaic

: having frequent or familiar association 2 archaic: CONCERNED. Oc
CUPIED 3: having knowledge or experience — used with with

con-ver-sa-tion \kän-vər-\sā-shən\ n [ME conversacioun, fr. MF con
con-ver-sa-tion \kän-vər-\sā-shən\ n [ME conversacioun, fr. MF con-

conver-sa-tion \kan-var-'sa-shan\ n [ME conversacioun, ir. MF conversation, fr. L conversation-conversatio, fr. conversatio associate with, freq. of convertere to turn around [14c) 1 obs: CONDUCT, BEHAVIOR 2 a (1): oral exchange of sentiments, observations, opinions, or ideas (2): an instance of such exchange: TALK b: an informal discussion of an issue by representatives of governments, institutions, or groups c: an exchange similar to conversation — conver-sa-tion-ally adv

shan'l adj — conver-sa-tion-ally adv

conversation-allist \shankshaplist \shanksh

-sno-ni\ aaj — con-ver-sa-tion-al-ist n (1836): one who conver-sa-tion-al-ist\ -sho-list, -sho-n³-ist\ n (1836): one who converses a great deal or who excels in conversation conversation piece n (1712) 1: a painting of a group of persons in their customary surroundings 2: something (as a novel or unusual object) that stimulates conversation

con-ver-sac-i-o-ne \kän-vər-sät-s\end{a}-n\end{a}, k\over-s\end{a}n-vər-s\u00e4t-s\end{a} \\-1\over-s\u00e4t-s\ : a meeting for conversation esp. about art, literature, or science | con-verse \kan-,vərs\ n (15c) | 1 obs: social interaction | 2: CONVER-

²con-verse \kən-'vərs\ vi con-versed; con-vers-ing [ME, to live (with), fr. MF converser, fr. L conversari] (1586) 1 archaic a: to become occupied or engaged b: to have acquaintance or familiarity 2 a: to exchange thoughts and opinions in speech: TALK b: to carry on an exchange similar to a conversation (as with a computer)—

2 a: to exchange similar to a conversation (as with a computer)—
converse \\'vor-sar\ n
converse \\'kän-\vor-sar\ n
converse \\'kan-\vor-sar\ n
converse \\'kan-\vor-sar\

conversion reaction n (1945): a psychoneurosis in which bodily symptoms (as paralysis of the limbs) appear without physical basis —

symptoms (as paralysis of the limbs) appear without physical basis—called also conversion hysteria

con-vert \kon-\vort \ vb [ME, fr. MF convertir, fr. L convertere to turn around, transform, convert, fr. com- + vertere to turn — more at worth] vt (14c) 1 a: to bring over from one belief, view, or party to another b: to bring about a religious conversion in 2 a: to alter the physical or chemical nature or properties of esp. in manufacturing b (1): to change from one form or function to another (2): to alter b (1): to change from one form or function to another (2): to alter for more effective utilization (3): to appropriate without right c: to exchange for an equivalent 3 obs: TURN 4: to subject to logical conversion 5 a: to make a goal after receiving (a pass) from a teammate b: to score on (as a try for point or free throw) c: to make (a

\a\ abut \a\ kitten, F table \ar\ further \a\ ash \a\ ace \a\ mop, mar \au\out \ch\chin \e\ bet \e\ easy \g\ go \i\ hit \i\ ice \j\ job \n sing $\\bar{0}$ go $\\bar{0}$ law $\\bar{0}$ boy \th thin \th the $\\bar{0}$ loot $\\bar{0}$ foot at the table minter to be a me me to N con Guide to Pronunciation